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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,111	04/26/2001	Kathleen D. Danenberg	11220/128	6762

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,111	DANENBERG, KATHLEEN D.	
	Examiner	Art Unit	
	Jeffrey Fredman	1634	

-- Th MAILING DATE of this communication appears on th cover she t with th correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11,17-22 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-11, 17-22, 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7, 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112 – Written Description

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 6-11, 17-22, and 26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

All of these claims encompass nucleic acids which are different from those disclosed in the specific SEQ ID Nos, which include variants for which no written description is provided in the specification. Specifically, the claims encompass "80% identical" oligonucleotides, but the specification give only certain specific oligonucleotides as examples of such primers and probes.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

"In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06

(discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, a certain subset of specific SEQ ID NOs is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception or description of any nucleic acids which are substantially identical to SEQ ID Nos: 1, 2, 7 and 8. This larger genus encompasses, according to the definition of the specification, anything which is at least 80% homologous with possible insertions and deletions. For example, with regard to SEQ ID NO: 1, which is 19 nucleotides in length, this would result in a requirement that only 80% or 16 nucleotides be constant. There are nearly a million such possible oligonucleotides. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Response to Arguments – Written Description

Applicant's arguments filed October 14, 2003 have been fully considered but they are not persuasive.

Applicant provides a discussion of the written description requirement. Applicant cites a particularly apropos part of Enzo, which notes that the function of the nucleic acid must be correlated to a "structure that is sufficiently known or disclosed". Applicant first argues, with regard to the written description rejection, that the current claims have structure and function. However, in the current case, the function is not correlated or tied to the structure, because percent homology of a sequence of the primers provides no structural requirements on the primer sequences themselves.

The distinction can be easily seen by comparison with the obviousness rejection below. That rejection, consistent with In re Deuel and In re Bell, does not rely upon any unknown sequences but relies instead upon specific prior art sequences from which the DPD primers are derived. There is no unknown sequence, there is no undescribed sequence, there is no percent homology or lack of detail. The prior art provides the DPD sequence in its entirety. To further clarify, if the prior art sequence of the DPD gene is GCAAGGAGGGTTTGTCACTG, the ordinary practitioner would recognize DPD specific primers with 100% matches to this sequence, such as GCAAGGAGGG, for example, which matches the first 10 nucleotides.

However, the current claims are not drawn simply to sequences selected from the DPD sequence, but expressly include sequences which are 80% homologous to those sequences. There is no structural feature to which the changes permitted by the

"80% homologous" language can be tied because no motifs or other elements are required. In the written description guidelines, the examples of functional language relate to required structural motifs which guide the practitioner in altering the molecules. The current functional language does not provide guidance on changes, since there are no motifs which need be conserved. Here the function, amplification, is available to any sequence whatever. That is, any sequence mixed with exon 1 of DPD would be "capable" of amplifying that sequence to some extent. For example, random hexamers are frequently used for such amplifications. Therefore, the function identified by Applicant is not sufficient to distinguish the primer requirements in any meaningful way.

Further, to directly respond to Applicant's citation of the written description guidelines, and in particular, Example 9, Applicant's quotation (and bolding) of the statement that "[A] person of skill in the art **would not expect substantial variation**" fails to recognize a central salient fact of the example. In example 9, the molecule at issue is not a primer whose sole function is hybridization but rather is a nucleic acid drawn to a full length protein, which binds to dopamine receptor and which stimulates adenylate cyclase activity (see example 9 of the guidelines). In this example, the claim is constrained by a very significant functional limitation, that members of the genus of nucleic acid which results must still encode a protein, that the encoded protein must still bind the dopamine receptor and that upon binding, adenylate cyclase activity must be stimulated. This is a very specific function for the protein which strongly delimits the nucleic acids. This is entirely unlike the current case where the functional limitations are all embedded in the nucleic acids themselves. That is, the limitations of 80% identity,

stringent hybridization and capable of amplifying do not really distinctly impact the structure of the primer. In the protein case of Example 9, the nucleic acid must encode the protein, therefore indicating that no stop codons were permitted, the protein must retain binding ability, meaning that very the binding domain must be unaffected and must activate adenyl cyclase, which is drawn to the activation domain of the protein. In the current case, an oligonucleotide which has 80% identity will inherently hybridize under stringent conditions and any oligonucleotide with two nucleotides of identity at the 3' end to the DHPD target will function to amplify that sequence. So these "distinct" limitations are, in fact, simply different ways to say the same functional requirement, that the oligonucleotide hybridize. So in fact, there is no distinct function claimed, unlike in example 9 where the nucleic acid was significantly constrained by function.

Applicant repeatedly argues that a combination of both prongs of the analysis would overcome the written description rejection. However, Applicant's analysis under the two prongs is similarly flawed for the reasons indicated above. There is no expectation in the instant case of insubstantial variation because the functional limitation devolves to the ability of the nucleic acid to hybridize. However, hybridization is an inherent capability of nucleic acids, and amplification, in particular, can be achieved with non specific primers. Many methods, ranging from ARMS to differential display, specifically rely on the fact that nonspecific unrelated nucleic acids are capable of amplifying specific targets. So the argument by Applicant that there would be insubstantial variation is not correct since the function of hybridizing and amplifying does not limit the nucleic acid in any significant way. As noted previously, random

hexamers would be capable of meeting the claim limitation of amplifying the target nucleic acid.

With regard to the second prong, Applicant lacks any coding function in the claim. Applicant's function is not distinct from the hybridization function of nucleic acids. Amplification depends upon and requires hybridization prior to extension. So there is no correlative function in the instant case for the claimed DPD primers.

Applicant makes the argument that the size of the genus is not relevant, arguing based upon teachings in the specification. This is not found persuasive because the size of the genus is a central issue. If the genus were small, a written description rejection would be less likely, since the examples would be more representative of the genus. Applicant argues that stringent hybridization is a structural requirements. This is not correct. These are functional limitations on the structure. That is, there is no specific structure required by stringent hybridization. All that these limitations require is oligonucleotides which are able to hybridize, whatever structure is present. With regard to the 80% limitation, for four changes, or 80% homology, the result would be (60 + (60 x 57) + (60 x 57 x 54) + (60 x 57 x 54 x 51) which equals 9, 606, 840 different possible configurations. This is an extremely substantial variation. Even with stringency conditions, this does not substantially reduce the size of the undescribed genus of over 9 million different possible oligonucleotides, for which Applicant has identified only 1.

Here, where the genus includes more than 9 million possible molecules, for which Applicant has selected one, the argument that the single species is representative is not found persuasive.

Applicant then argues the citation of Lilly, noting that even if the protein homology were 80%, the nucleic acid sequences would be less than 80% identical. In fact, this statement is not correct. As the blast alignment of the human insulin mRNA gene (Genbank Accession Number NM_000207) against the rat insulin gene (Genbank Accession Number J00747) below shows, the homology is actually 81% between the nucleic acid sequences which encode rat and human insulin. So Applicant's entire argument on page 31 is based on an incorrect presumption, which is that the 80% alignment is of proteins, not nucleic acids. Applicant also argues that the insufficient homology was not the reason the claims were held invalid, but rather because there was no disclosure of the human protein. However, this argument is incorrect if 80% homology, such as that claimed by Applicant, is sufficient to describe the genus. Since the nucleic acid of rat insulin, which was disclosed, was more than 80% homologous to the human insulin, by Applicant's argument previously, that disclosure should have been sufficient to describe the genus which encompassed the human insulin. However, the court in Lilly disagreed, and found that the disclosure of an 80% homologous sequence was insufficient to meet the written description requirement.

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Score =  281 bits (146), Expect = 8e-73
Identities = 270/332 (81%)
 Strand = Plus / Plus


Query:          44   catggccctgtggatgcgcctcctgcccctgctggcgctgctggccctctggggacctga 103
                     |||||||||||||||||| |||||||||||||||| ||||| | ||||||||  ||  |
Sbjct:          4181 catggccctgtggatgcgcttcctgcccctgctggccctgctcgtcctctgggagcccaa 4240
preproinsulin I 1      M  A  L  W  M  R  F  L  P  L  L  A  L  L  V  L  W  E  P  K

Query:          104  cccagccgcagcctttgtgaaccaacacctgtgcggctcacacctggtggaagctctcta 163
                      || |||   || ||||| || || ||||| || ||  | |||||||||||| ||||| ||
Sbjct:          4241 gcctgcccaggcttttgtcaaacagcacctttgtggtcctcacctggtggaggctctgta 4300
preproinsulin I 21     P  A  Q  A  F  V  K  Q  H  L  C  G  P  H  L  V  E  A  L  Y
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Query:          164  cctagtgtgcggggaacgaggcttcttctacacacccaagacccgccgggaggcagagga 223
                     ||| ||||| |||||||| || ||||||||||||||||| |||| || || |  |||||
Sbjct:          4301 cctggtgtgtggggaacgtggtttcttctacacacccaagtcccgtcgtgaagtggagga 4360
preproinsulin I 41     L  V  C  G  E  R  G  F  F  Y  T  P  K  S  R  R  E  V  E  D


Query:          224  cctgcaggtggggcaggtggagctgggcgggggccctggtgcaggcagcctgcagccctt 283
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Sbjct:          4361 cccgcaagtgccacaactggagctgggtggaggcccggaggccggggatcttcagacctt 4420
preproinsulin I 61     P  Q  V  P  Q  L  E  L  G  G  G  P  E  A  G  D  L  Q  T  L


Query:          284  ggccctggaggggtccctgcagaagcgtggcattgtggaacaatgctgtaccagcatctg 343
                     ||| |||||||   ||| ||||||||||||||||||||| || ||||| ||||||||||
Sbjct:          4421 ggcactggaggttgcccggcagaagcgtggcattgtggatcagtgctgcaccagcatctg 4480
preproinsulin I 81     A  L  E  V  A  R  Q  K  R  G  I  V  D  Q  C  C  T  S  I  C


Query:          344  ctccctctaccagctggagaactactgcaact 375
                     |||||||||||| ||||||||||||||||||
Sbjct:          4481 ctccctctaccaactggagaactactgcaact 4512
preproinsulin I 101    S  L  Y  Q  L  E  N  Y  C  N  ^
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Applicant argues that any sequence would not amplify DPD genes, as argued earlier in the final rejection. Applicant is directed to the well known in the art technique of synthesizing probes using random hexamers. Here a pool of every random six nucleotide long oligonucleotide is mixed with a target nucleic acid and invariably results in an amplified product which is labeled with the desired radioactive label. As Applicant is likely well aware, this technique is simply one of many, ranging from ARMS to differential display, which rely upon arbitrary or random sequences to specifically amplify genes. Applicant's argument that random hexamers would never be used for PCR. This is simply not correct, as shown by Peng et al, "Multiple PCR analyses on trace amounts of DNA extracted from fresh and paraffin wax embedded tissues after random hexamer primer PCR amplification", J. Clin. Pathol. 47(7):605-8, where Peng's title makes clear that he performs PCR with random hexamers. As a side point, Peng even is performing the method in archival paraffin wax tissue sections with success,

suggesting that longer primer such as those of Gonzalez would be readily expected to be successful.

Applicant concludes this section by reiterating arguments on Example 9 that have already been addressed above and that are not persuasive.

Therefore, the argument is not found persuasive.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 6-11, 17-22, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al (U.S. Patent 6,015,673) in view of Willhauck et al (Biotechniques (1998) 25:656-659).

Gonzalez teaches a method for determining the level of DPD gene expression in a tissue to determine the safety of a 5-fluorouracil based chemotherapeutic regimen comprising the steps: (see column 14, lines 41-51, also see column 27, lines 14-27, here the tissue is cultured fibroblasts derived from skin biopsies),

(a) obtaining a sample from a patient (column 14, lines 41-52)

(b) isolating mRNA from the sample (column 14, lines 52-67),

(c) amplifying the mRNA with primers which are substantially identical to SEQ ID NO: 1 and 2 (see column 55, SEQ ID NO: 5)

a sequence, SEQ ID NO: 5, which is a sequence substantially identical to the claimed SEQ ID NO: 1 as shown in the alignment below.

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Gonzalez SEQ ID NO: 5 -   GCAAGGAGGGTTTGTCACTG
                          ||||||||||||||||
Claimed SEQ ID NO: 1 AGGACGCAAGGAGGGTTTG
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As the alignment shows, the Gonzalez sequence is 14/19 nucleotides identical to the claimed sequence, for a homology over the claimed sequence of 73%. Further, all of the SEQ ID NO:s are substantially identical to the human DPD sequence disclosed in SEQ ID NO: 1 of U.S. Patent 5,856,454 and are derived from that sequence. Gonzalez teaches the full sequence from which the primers were derived.

Gonzalez teaches freezing of the sample (see column 25, line 64) as well as fixing of the sample for detection (see column 13, lines 46-53).

Gonzalez teaches isolation of mRNA in the presence of Guanidine, a chaotropic agent (column 14, lines 52-67).

Gonzalez teaches that appropriate samples include any cells from the patient that may express the DPD gene (column 14, lines 41-51).

Gonzalez teaches a threshold for the mutation in which there is a problem tolerating 5-fluorouracil based chemotherapeutic regimens where a 2 fold difference will yield enhanced risk (see column 15, lines 1-11)

Gonzalez does not teach step (d) comparing the amount of DPD mRNA to the amount of mRNA of an internal control gene.

Willhauck teaches comparing the amount of the target gene to an internal control gene (see page 656, columns 1-3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the internal controls of Wilhauck in the method of Gonzalez since Wilhauck states "Taken together our results show that the internal control circumvents a number of inherent problems of alternative controls to assess pre-PCR procedures. The overall RT-PCR assay sensitivity can be reliably evaluated on a per sample basis and the sensitivity limit of the RT-PCR assay can be assessed for every sample. This type of reliability can improve the homogeneity of results from clinical investigations in the future (page 658, column 3 to page 659, column 1)". An ordinary practitioner would have been motivated to use the internal controls of Wilhauck in the method of Gonzalez in order to reliably and sensitively improve the homogeneity of the clinical results.

Response to Arguments – Prior art Rejections

5. Applicant's arguments filed October 14, 2003 have been fully considered but they are not persuasive.

Applicant argues that there would be no motivation to select the specific, slightly adjusted primers claimed. In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

> "Normally, a *prima facie* case of obviousness is based upon structural similiarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have

> similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the Gonzalez prior art as useful for primers and probes for the detection of DPD, and in particular for diagnosis of whether to use 5-fluorouracil, and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Applicant argues that Gonzales does not teach primers which are 80% identical to the specific primers claimed. While that is correct, Gonzalez teaches primers selected from the same gene for the same purpose. The complete gene sequence is taught by Gonzalez, a sequence which comprises the regions that are 100% identical to the claimed sequence. Thus, selection of a particular sequence from the larger sequence is prima facie obvious. This supports the argument that the primers of Gonzales are equivalent to those claimed and represent homologs as per Deuel.

Applicant concludes by arguing that there is no motivation to use primers to amplify the DPD sequence. This is simply incorrect. Gonzalez provides abundant motivation to amplify the DPD sequence. Gonzalez teaches that detection of the level of DPD gene expression may be a controlling feature of the toxicity of 5-fluorouracil, a chemotherapeutic agent. Thus, an ordinary practitioner would have been motivated to amplify the DPD gene in order to monitor whether the drug level proposed for a particular patient would be toxic. In particular, it is desirable to maximize efficacy of the drug while minimizing toxicity, so Gonzalez teaches that the amplification of DPD permits patient specific dosing, which will maximize therapeutic effect.

Consequently, the prior art rejection is maintained.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner

JEFFREY FREDMAN
PRIMARY EXAMINER